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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ROBERT BOIZEL, PASCALE FOUQUERAY,
DANIEL GUERRIER, JEAN-JACQUES ZEILLER,
and BERTRAND BRUTZKUS

Appeal 2009-005158
Application 10/580,602
Technology Center 1600

Decided: December 2, 2009

Before ERIC GRIMES, FRANCISCO C. PRATS, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method for preventing or treating hyperuricemia. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

Statement of the Case

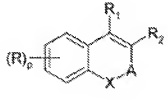
Background

"Hyperuricemia is a metabolic disturbance that may lead to gout, which is a commun [sic, common] medical problem, affecting at least 1 percent of men in Western countries" (Spec. 2, ll. 10-12). The Specification notes that "[h]yperuricemia is associated with cardiovascular impairment over the long term. Recent epidemiological studies have shown that an elevated uric acid is a common feature of the metabolic syndrome, which confers an increased risk for the development of hypertension, ischemic heart disease and stroke" (Spec. 3, ll. 19-24).

The Claims

Claims 1-6, 8-11, 13-19, 23-25, and 35-41 are on appeal[1]. We will focus on claim 1, which is representative and reads as follows:

> 1. A method for preventing or treating hyperuricemia; or for treating a disorder associated with hyperuricemia; or for reducing the serum uric acid level of a subject, comprising administering to a subject in need thereof a compound of formula (I)



(I)

> in which:
> X is O or S;

[1] The Examiner withdrew claims 7, 12, and 34 from consideration based upon a restriction requirement.

A is a divalent radical $-(CH_2)_s-CO-(CH_2)_t-$ or $-(CH_2)_s-CR_3R_4-(CH_2)_t-$, in which s = t = 0 or one of s and t has the value 0 and the other has the value 1;

R_1 and R_2 are, each independently; a hydrogen atom; a (C_1-C_{18})alkyl group; a (C_2-C_{18})alkenyl group; a (C_2-C_{18})alkynyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group; a (C_1-C_{18})alkyl group; a (C_2-C_{18})alkenyl group; a (C_2-C_{18})alkynyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group;

R_3 and R_4 are, each independently, a hydrogen atom; a (C_1-C_{18})alkyl group; a (C_2-C_{18})alkenyl group; a (C_2-C_{18})alkynyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group; a (C_1-C_{18})alkyl group; a (C_2-C_{18})alkenyl group; a (C_2-C_{18})alkynyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group; or

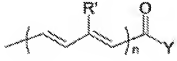
R_3 and R_4 together form a (C_2-C_6)alkylene chain optionally substituted by a halogen atom or by optionally halogenated (C_1-C_5)alkoxy;

R is a halogen atom; a cyano group; a nitro group; a carboxy group; an optionally halogenated (C_1-C_{18}) alkoxycarbonyl group; an R_a-CO-NH- or R_aR_bN-CO- group; an optionally halogenated (C_1-C_{18})alkyl group; optionally halogenated (C_1-C_{18})alkoxy; and (C_6-C_{10})aryl, (C_6-C_{10})aryl(C_1-C_5)alkyl, (C_6-C_{10})aryloxy, (C_3-C_{12})cycloalkyl, (C_3-C_{12})cycloalkenyl, (C_3-C_{12})cycloalkyloxy or (C_3-C_{12})cycloalkenyloxy, in which the aryl, cycloalkyl or cycloalkenyl group is optionally substituted by a halogen atom, by optionally halogenated (C_1-C_5)alkyl or by an optionally halogenated (C_1-C_5)alkoxy; -OH;

R_a and R_b are, each independently, an optionally halogenated (C_1-C_{18})alkyl; a hydrogen atom; (C_6-C_{10})aryl or (C_6-C_{10})aryl(C_1-C_5)alkyl, in which the aryl group is optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group); (C_3-C_{12})cycloalkyl optionally substituted by a halogen atom, by an optionally halogenated C_1-C_5 alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group;

P is 0, 1, 2, 3 or 4;

Z is:

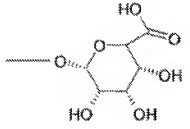


n is 1 or 2;

R' are, each independently, a hydrogen atom; a (C_1-C_5)alkyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by optionally halogenated (C_1-C_5)alkoxy; or a mono- or bicyclic (C_4-C_{12})heteroaryl group containing one or more O, N and/or S atoms, which is optionally substituted by halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group;

Y is -OH; (C_1-C_5)alkoxy; or -NR_cR_d;

or gluco[n]ic acid



R_c and R_d are, each independently, a hydrogen atom; (C_1-C_5)alkyl; (C_3-C_8)cycloalkyl optionally substituted by a halogen atom, by optionally halogenated (C_1-C_5)alkyl or by optionally halogenated (C_1-C_5)alkoxy; (C_6-C_{10})aryl

optionally substituted by a halogen atom, by optionally halogenated (C_1-C_5)alkyl or by optionally halogenated (C_1-C_5)alkoxy;

wherein one, and one alone, of R_1 and R_2 is Z;

or a pharmaceutically acceptable salt thereof with a acid or base, or an ester thereof.

The prior art

The Examiner relies on the following prior art references to show unpatentability:

Brunet et al	WO 00/39113 A1 Jul. 6, 2000
Chen et al.	WO 00/47209 A1 Aug. 17, 2000

The issue

The Examiner rejected claims 1-6, 8-11, 13-19, 23-25, and 35-41 under 35 U.S.C. § 103(a) as obvious over Brunet and Chen (Ans. 3-5).

The Examiner finds that "Brunet et al. teach compounds of the same core structure as the instant application. The compounds are powerful activators of the PPARα and PPARγ isoforms[2] and exhibit hypolipidaemic and hypoglycaemic effects" (Ans. 3-4). The Examiner finds that "Chen et al. teach that activators of PPARγ are uricosuric agents which are useful for the treatment of gout and related disorders" (Ans. 4). The Examiner concludes that it would have been obvious to "use the compounds of Brunet et al. for the treatment of hyperuricemia and associated disorders . . . because Chen et al. teach that activators of PPARγ are useful for the treatment of

[2] "PPAR" refers to "Peroxisome Proliferator Activated Receptors" (*see* Brunet 2).

gout and related disorders and the compounds of Brunet et al. are taught to be powerful activators of PPARγ"(Ans. 5).

Appellants contend that "[n]othing in WO '209 teaches or suggests that the compounds therein having activity on PPARγ only should be replaced with compounds which are dual activators, i.e., compounds which activate PPARα and PPARγ, to achieve the treatment of diseases associated with hyperuricemia" (App. Br. 3). Appellants further contend that "[n]othing in either reference teaches or suggests that compounds which are structurally completely different and have different activity profiles as discussed above should or even could be used interchangeably to achieve a desired result, e.g., the claimed method" (App. Br. 3).

In view of these conflicting positions, we frame the obviousness issue before us as follows:

Have Appellants demonstrated that the Examiner erred in concluding that it would have been obvious to use the PPARα and PPARγ activator compounds of Brunet as PPARγ uricosuric agents in the treatment of hyperuricemia as taught by Chen?

Findings of Fact (FF)

1. Brunet teaches "a new class of compounds which are powerful activators of the PPARα and PPARγ isoforms. Due to this activity, these compounds exhibit a significant hypolipidaemic and hypoglycaemic effect" (Brunet 2, ll. 15-19).

2. The Examiner finds that Brunet teaches "as an exemplary compound [page 34, lines 12-15] and preferred species [page 10, lines 9 and 10] is Example 16b, (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-

dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid, which is the species which applicant has elected in the instant application" (Ans. 4)

3. Brunet teaches that the compounds are "intended to prevent or treat dyslipidaemias, atherosclerosis or diabetes. The hypolipidaemic and hypoglycaemic activity of the compounds of the invention was demonstrated in vitro and in vivo" (Brunet 33, ll. 13-17).

4. Brunet teaches that the elected compound activated PPARα and PPARγ in a luciferase transfection system (Brunet 33-34).

5. Brunet teaches treatment of db/db mice with the exemplary compound and teaches that "[t]hese results unambiguously demonstrate the hypolipidaemic and antidiabetic activity of the compounds of the invention" (Brunet 35, ll. 9-11).

6. Chen teaches that "[h]yperuricemia, however, is the key feature of gout and is a result of either an increased production of urate or a decreased excretion of uric acid, or potentially a combination of both processes" (Chen 1, ll. 25-27).

7. Chen teaches that "activators of peroxisome proliferator-activated receptor γ (PPARγ) are also uricosuric agents and are useful for the treatment of gout and related disorders" (Chen 2, ll. 31-33).

8. Chen teaches that "[s]urprisingly, a broad spectrum of PPARγ ligands were found to also be uricosuric agents, establishing this mechanism as one avenue for the control of gout and other hyperurocemic diseases" (Chen 7, ll. 8-10).

Principles of Law

The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). The Supreme Court has recently emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

Analysis

Brunet teaches compounds which "are powerful activators of the PPARα and PPARγ isoforms" (Brunet 2, ll. 15-19; FF 1). Chen teaches that "activators of peroxisome proliferator-activated receptor γ (PPARγ) are also uricosuric agents and are useful for the treatment of gout and related disorders" (Chen 2, ll. 31-33; FF 7). Chen teaches that "[s]urprisingly, a broad spectrum of PPARγ ligands were found to also be uricosuric agents, establishing this mechanism as one avenue for the control of gout and other hyperurocemic diseases" (Chen 7, ll. 8-10; FF 8).

We agree with the Examiner's reasoning that it would have been obvious to "use the compounds of Brunet et al for the treatment of hyperuricemia . . . because Chen et al. teach that activators of PPARγ are useful for the treatment of gout . . . and the compounds of Brunet et al. are taught to be powerful activators of PPARγ" (Ans. 5). An obviousness

"analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418.

We are not persuaded by Appellants' argument that "[n]othing in WO '209 teaches or suggests that the compounds therein having activity on PPARγ only should be replaced with compounds which are dual activators, i.e., compounds which activate PPARα and PPARγ, to achieve the treatment of diseases associated with hyperuricemia" (App. Br. 3). Chen expressly teaches that "a broad spectrum of PPARγ ligands were found to also be uricosuric agents" (Chen 7, ll. 8-10; FF 8), which provides a direct suggestion to use compounds such as Brunet's which target PPARγ in the treatment of hyperurocemia. The fact that the compounds of Brunet may have additional activities does not detract or teach away from their use in the treatment of hyperuricemia, but may simply permit them to be useful for other diseases or indications as well.

We do not find persuasive Appellants' argument that "[n]othing in either reference teaches or suggests that compounds which are structurally completely different and have different activity profiles as discussed above should or even could be used interchangeably to achieve a desired result, e.g., the claimed method" (App. Br. 3). Chen teaches that a variety of structurally different compounds function interchangeably as uricosuric agents, which directly addresses Appellants' argument (FF 8).

We are not persuaded by Appellants' argument that "one of ordinary skill in the art would have lacked a reasonable expectation of success in

achieving the treatment, e.g. of hyperuricemia with the compounds of WO '113" (App. Br. 3). *Kubin* commented that "[r]esponding to concerns about uncertainty in the prior art influencing the purported success of the claimed combination, this court [in *O'Farrell*] stated: '[o]bviousness does not require absolute predictability of success … all that is required is a reasonable expectation of success."' *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009) (*citing In re O'Farrell*, 853 F.2d 894, 903-904 (Fed. Cir. 1988)). We find that Chen provides clear guideposts and explicit suggestion on which compounds will function in the treatment of hyperuricemia, specifically suggesting compounds which activate PPARγ (FF 7-8). Combined with Brunet's teaching of specific compounds which both activate PPARγ and are functional in therapeutic settings, use of Brunet's PPARγ activating compound for treatment of hyperuricemia as disclosed by Chen represents a "reasonable expectation of success" situation where there was a predictable solution and a finite number of identified compounds which activate PPARγ (FF 1-8).

Conclusion of Law

Appellants have not demonstrated that the Examiner erred in concluding that it would have been obvious to use the PPARα and PPARγ activator compounds of Brunet as PPARγ uricosuric agents in the treatment of hyperuricemia as taught by Chen.

SUMMARY

In summary, we affirm the rejection of claim 1 as obvious under 35 U.S.C. § 103(a) over Brunet and Chen. Pursuant to 37 C.F.R. §

41.37(c)(1)(vii)(2006), we also affirm the rejections of claims 2-6, 8-11, 13-19, 23-25, and 35-41 as these claims were not argued separately.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

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